Pediatric RESEARCH

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COMMENT

Classifying by cause and preventing the many causes of spina bifida and anencephaly

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A vast majority of pregnancies affected by spina bifida and anencephaly are attributed to known causes. It is important to give a short name and to focus on each cause because prevention requires different interventions depending on the cause. Knowing the proportion of cases attributable to each cause can also help in setting priorities for interventions, especially where resources are limited. In addition, monitoring by specific cause can identify failures in prevention programs and practice that require improvement. Giving short names to these causes is also a reminder that we do know causes and that we can stop introducing papers by using the boilerplate words that spina bifida and anencephaly are caused by the multifactorial interplay of genetic and environmental influences—the classic words we use to try to cover our ignorance of causes.

A good analogy for naming the kinds of spina bifida and anencephaly by their cause can be drawn from hepatitis and polio. It is common practice to classify hepatitis cases under Type A, B, C, D, or E depending on the type of causal virus. Similarly, polio is classified as Type 1, 2, or 3 depending on the type of virus. Such classification allows interventions that are specific. I propose that a similar approach should be used for spina bifida and anencephaly, using labels that indicate etiology.

SPINA BIFIDA F AND ANENCEPHALY F

Inadequate blood folate concentration among women of reproductive age is the predominant cause of spina bifida and anencephaly globally.[1] These types of folic acid-preventable spina bifida and anencephaly should be named as Spina Bifida F and Anencephaly F, respectively.

One of the most important inferences after mandatory, mass population-wide folic acid fortification is that the non-folic acid preventable spina bifida and anencephaly occur at 5 per 10,000 births in all countries studied so far. The expected percentage reduction in prevalence after fortification will vary depending upon the before fortification rates of spina bifida and anencephaly. For example, in Ethiopia, the before rate is 130 per 10,000 births.[2] Required mass fortification of food with folic acid, when implemented effectively and reaching all in the country, would prevent 96% (125/130)) of spina bifida and anencephaly within a year of implementation. In the United States, on the other hand, the reduction was around 50% from pre-fortification rate of 10 to post-fortification rate of 5 per 10,000 births.[3] In Canada, the percentage reduction varied from 90% in Newfoundland to 50% in Ontario.[4]

Another key inference is that every country, without mandatory large-scale food fortification programs with folic acid, has an epidemic of spina bifida and anencephaly. The magnitude of the epidemics, of course, varies by country. It follows that countries which do not have mandatory folic acid fortification programs, such as those in Europe, Africa, and Asia, should move rapidly to implement mass folic acid fortification without spending more time and money on research studies. We know enough about the safety and effectiveness of mass folic acid fortification to justify immediate fortification in all countries even though we may not know, for example, how much prevention to expect or how much of the fortified food will be eaten. Perhaps most important, we know that every day's delay in mass folic acid fortification will be a day for which the epidemic continues to give children and families preventable, life-altering conditions. Assessment of blood folate concentrations after fortification can rapidly tell whether the concentrations of required folic acid fortification need to be adjusted or additional foods fortified.

One of the most tragic public health failures of our time is the failure of the United Kingdom to require mass folic acid fortification of flour. Tax dollars supported the UK Medical Research Council study that, in 1991, unequivocally proved that folic acid prevents Spina Bifida F and Anencephaly F.[5]

Required mass folic acid fortification was implemented in 1998 in the United States and Canada. Post-fortification studies have shown folic acid fortification to be safe and to prevent not only spina bifida and anencephaly but also folate deficiency, folate deficiency anemia, and elevated homocysteine concentrations. In addition to saving lives, mass fortification in the United States has saved $150 for every $1 it cost. The failure to implement required, mass folic acid fortification of flour has meant that the citizens of the United Kingdom, for 28 years, have not benefited, as have Americans, Canadians, and Australians, from the research they paid for.

SPINA BIFIDA V

Valproic acid was shown to cause Spina Bifida V, but not anencephaly, in France in 1982.[6] The addition of concerns about an increase in total major congenital anomalies and cognitive impairment from in utero exposure has led US Food and Drug Administration and other health authorities to increase the strength of the warnings for women of reproductive age.[7,8] Nevertheless, the drug remains on the market in many countries, including the United States, France, and the United Kingdom, leaving unmeasured toll of death and disability from spina bifida.

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Valproic acid is approved not only for epilepsy but also for migraine headaches and psychiatric disorders.

Pediatricians can play an important role in preventing Spina Bifida V. They can encourage regulatory authorities to constrict the approved uses and to advocate that any woman of reproductive age also be on a highly effective contraceptive like implantable or intrauterine device. No girl or woman of reproductive age should be started on valproic acid as a first-line drug. Those who are known to be on the drug should be encouraged to discuss the possibility of other medication if they could become pregnant.

SPINA BIFIDA DM AND ANENCEPHALY DM

Women with insulin-dependent diabetes mellitus are at increased risk for having babies with major congenital anomalies, especially Spina Bifida DM and Anencephaly DM.[9] It is known that pregnancies with well-controlled diabetes remove most of the increased risk for congenital anomalies, although this well-known association has yet to be shown to be causal in randomized controlled studies.[10] Pediatricians who treat girls and young women with diabetes should help them develop a life-long habit of good glucose control for their own health and the health of any babies they may have.

OTHER TYPES

Currently, there are concerns about arsenic and fumonisin, as well as genetics, as potential risk factors for spina bifida and anencephaly. Should any of these potential factors be shown to be causal, they, too, will require an intervention that is specific. We will not be able to prevent all spina bifida until we know additional causes. While the search for the unknown causes continues, there is great need to give priority to preventing the causes we know about. Several of them are highly preventable through simple, easy, and cost-effective interventions.

SUMMARY

A majority of the world's burden from spina bifida and anencephaly is attributed to Spina Bifida F and Anencephaly F. There is an epidemic of these birth defects present in any country that does not have mandatory large-scale food fortification with folic acid or where policies/regulations exist but are not implemented well. Every country should immediately implement effective mandatory fortification of staple foods, such as wheat flour, rice, and salt. Medical interventions should limit valproic acid exposure and promote control of insulin-dependent diabetes among women of reproductive age. Inaction is unethical. Although the proportion of spina bifida and anencephaly from other causes is low, research to find unknown causes could inform additional prevention of these serious and life-threatening birth defects.

ADDITIONAL INFORMATION

Competing interests: The author declares no competing interests.

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